

Application No.: 09/989,991

Docket No.: 219002029100

**REMARKS**

Applicants first address the differences between with amendment now submitted and that submitted on 15 September.

In claim 1, in the definition of Ar, the term "fused" describing the ring formed by two optional substituents on adjacent positions has been retained, and not deleted as it was in the previously submitted amendment. It is believed that this overcomes the first objection set forth in the Advisory Action.

The criticism in the Advisory Action of claim 68 has been addressed by limiting the conditions to rheumatoid arthritis. This was the indication agreed upon in the copending application U.S. Serial No. 09/575,060 for which the issue fee has been paid. Thus, claim 68 as now proposed is identical to claim 42 in that application. If this amendment is not satisfactory, applicants hereby authorize the Examiner to cancel claim 68.

Finally, with respect to the definition of W and X contained in the definition of A, applicants respectfully point out that this definition was agreed upon as not indefinite in the application cited above in the context of an interview in that case, held 9 October 2003, between the undersigned and Examiner Chang. As Examiner Chang pointed out at the interview, once the substituents are defined as alkylene or alkenylene, the limitation on length simply dictates the number of carbons that is possible in the chain. This is not inconsistent with the definition of alkylene or alkenylene in the application for two reasons. First, although it may be the case that alkylene may contain 1-10C and alkenylene may contain 2-10C, the claim is directed to a subset of these more broadly defined categories. Thus, for example, simply because it is possible that alkenylene can contain 10C, it is not required that every time alkenylene is present in a structure it must be allowed to inhabit the full

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range. Thus, even if what the Office says is true – that alkylene of a length of 2-6 Å must have at least two carbons, there is nothing inherently wrong or inconsistent with such a requirement. The substituent in question is just limited to some, but not all possibilities for alkylene.

In fact, however, the alkylene may have only one carbon. The Examiner correctly states that the carbon-to-carbon chain length is 1.53 Å; however, for a single carbon to be present between two adjacent substituents, two such bonds are required:  $\text{--C--}$ . Thus, the total number of Angstroms is approximately 3. Four such bonds would sum to approximately 6 Å, and thus, the requirement for chain length translates into a 1-3 carbon chain:  $\text{--C--C--C--}$ .

Again, this is a subset of the possible embodiments of alkylene and alkenylene.

It is thus respectfully submitted that all three concerns which precluded the entry of the amendment have been addressed.

Turning now, to the amendments to which no objection was made, the explanation for these as set forth in the previous response is now repeated.

While applicants consider the terms “heteroalkyl”, “heteroalkenyl”, “heteroalkynyl” and “[hetero]forms thereof” to be clearly understood by those of skill in the art, and thus definite, those terms have been removed from the language of the amended claims in order to expedite prosecution. Each amended claim retains the list of specific substituents that was presented in the original claim and specification; thus the amended claims are fully supported by the original application and add no new matter.

All “noninterfering substituents” have been specifically defined in claim 1 and this term has been deleted. While applicants find this term as explained in the specification to be clear to one of ordinary skill, to give adequate notice of the scope of the claimed invention, and to claim the

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invention as conceived and understood by the inventors, it has nevertheless been defined structurally in each case to expedite prosecution. Each amended claim retains the list of specific substituents that was presented in the original claim and specification; thus the amended claims are fully supported by the original application and add no new matter.

As amended, the claims no longer recite or rely on any of the functional language to which the Examiner has objected: the claims recite clear and definite structural limitations to define the scope of the claimed invention. The Examiner's concern that one could not determine whether a given compound falls within the scope of the claims without making the compound and testing it has thus been addressed, and applicants believe the amended claims are definite and allowable.

The Examiner also mentions "issues about size and structure" and incorporates by reference the relevant comments from Papers No. 12 and 14; applicants are unsure whether this objection has been fully resolved by prior amendments. While most size-based claim limitations have been removed by previous amendment, claim 1 still defines one portion of the molecule by chain length where it states: "each of W and X is substituted or unsubstituted alkylene or alkenylene, each of 2-6 Å." As explained above, it is not clear to applicants why this would be considered indefinite. A specific chain length range is provided. The description in the specification clarifies how such lengths should be computed, when it describes  $L^1$  and  $L^2$ : the distance is measured with bond lengths placed end-to-end. As the Examiner has shown, specific bond lengths are readily found in the CRC Handbook of Chemistry and Physics, for example. One of ordinary skill would thus have no difficulty ascertaining which alkylene and alkenylene groups fall within the scope of the claims.

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Utility

The Examiner also questions whether the 'method of use' claims satisfy the utility requirement, since they recite alleviation of p38- $\alpha$  mediated conditions. Under the PTO Guidelines, the utility requirement is satisfied where *in vitro* enzyme activity is demonstrated as long as the target enzyme is associated with the disease state for which utility is asserted. The claimed compounds are inhibitors of p38, and especially p38- $\alpha$ . These enzymes are widely associated in the literature with specific disease states. Under *In re Brana*, the PTO has the burden to establish that one of ordinary skill would reasonably doubt the utility asserted by the applicant. 51 F.3d 1560 (Fed. Cir. 1995). The Examiner has not here provided a *prima facie* case to show that one of ordinary skill would *more likely than not* doubt the asserted utility of these compounds; thus the applicants believe such objection is not appropriate.

Nevertheless, the limitations in the method claims to p38- $\alpha$  mediated conditions has been eliminated by canceling claims 65-66 and re-writing claim 68 in independent form, claim 68 is further limited to treatment of rheumatoid arthritis.

Clerical Corrections

A typographical error in claim 1, which was repeated in claims 57 and 58, has been corrected by deletion of "alkyl-OOR" from the list of permitted groups for R<sup>3</sup> and R<sup>4</sup>.

Claim 12 has been made to depend from claim 1; it originally depended from claim 11 which has been canceled previously, and its dependency was not previously corrected.

Clarifying language was added to the description of R<sup>3</sup> in claim 57; support for this description of R<sup>3</sup> is found in the specification at page 13.

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Claim 68 has been rewritten in independent form, incorporating language from canceled claim 66.

Claims 40 and 41 have been modified to make them consistent with the present version of claim 1. Support for the narrower descriptions of L<sup>1</sup> and L<sup>2</sup> is found in the originally presented claims and in the specification.

Claims 42-43 and 64-67 have been canceled.

### CONCLUSION

It is believed that the present claims overcome the Examiner's stated objections and are free of the art. Therefore, it is respectfully requested that claims 1, 3-7, 9, 12, 39-41, 45-46, 48-50, 52-56, 57-61, 63 and 68 be deemed allowable and pass to issue forthwith.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket No. 219002029100.

Respectfully submitted,

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